

Building on our current treatments | *is precision medicine the future for cholangiocarcinoma?*

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Travel Grant

Celgene; NuCana; Pfizer

Speakers' Bureau

Imaging Equipment Ltd; Ipsen; Novartis; Nucana

Consulting or Advisory Role

Agios; AstraZeneca; Debiopharm; Delcath Systems;
GenoScience Pharma; Imaging Equipment Ltd; Incyte;
Ipsen; Keocyt; Merck; Mundipharma EDO; Novartis;
Nucana; PCI Biotech; Pieris Pharmaceuticals; Pfizer; QED;
Servier; Wren Laboratories

Every patient is an individual

Things we (as doctors) need to know:

1. About the cancer itself:

- What type of biliary tract cancer
- What “stage” is the cancer at?
- What treatment has already been given?
- Do we know about the molecular profile?
- Is there a clinical trial option?

2. About the patient

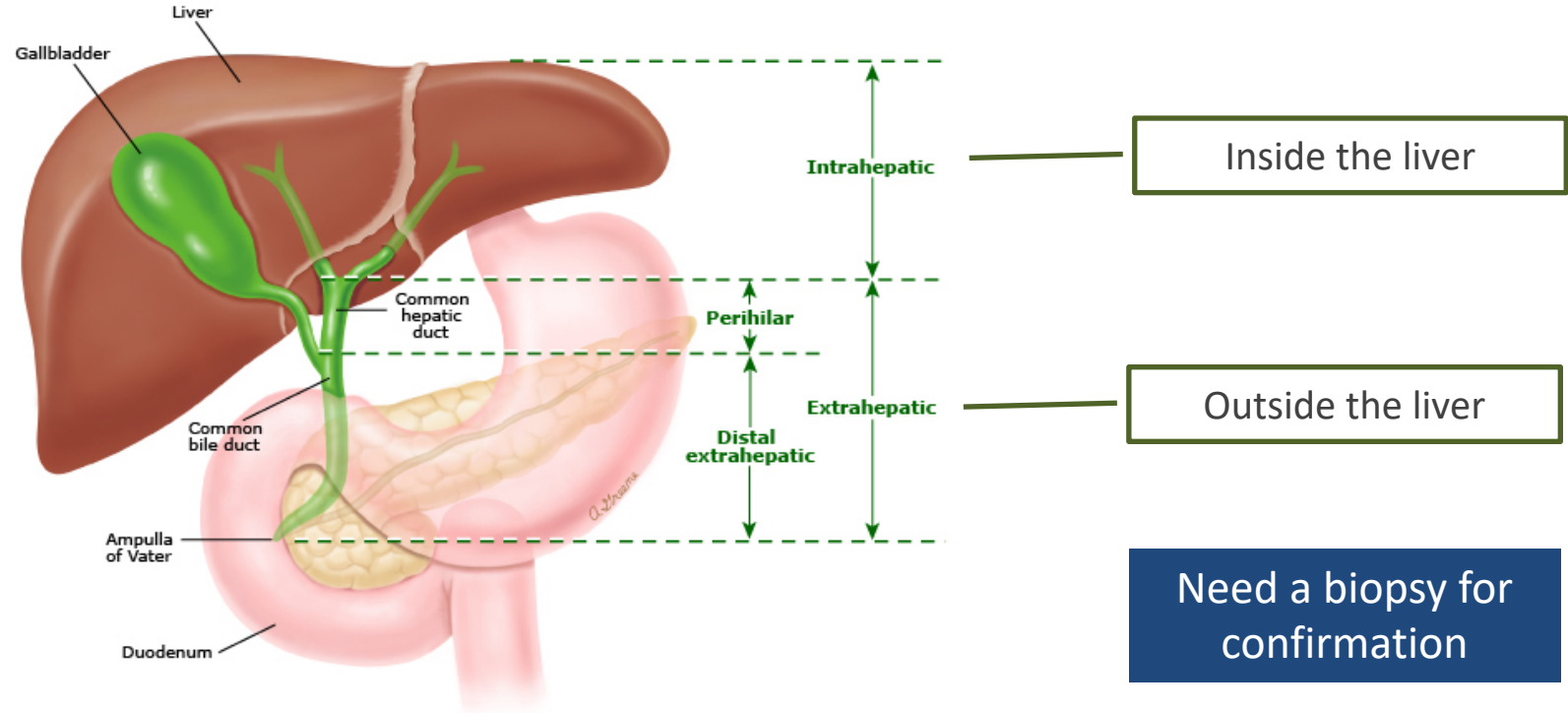
- Level of fitness (“performance status”)
- Other health problems
- Other medication
- Preferences

3. What are we trying to achieve?



What type of cholangiocarcinoma?

This question is about ANATOMY (part of the body) - “Where has the cancer started?”

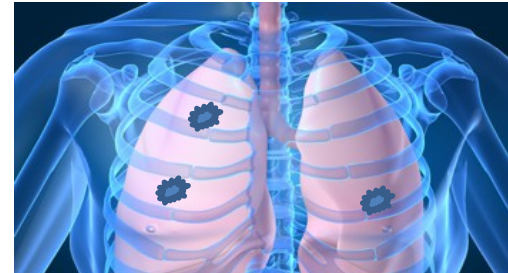


What stage is the cancer at?

Early

Locally
advanced

metastatic



How do we establish this?

- CT scan
- MRI scan
- Maybe a PET scan

About the patient...

Level of fitness (“performance status”)

Score

PS 0 – well and no symptoms at all

PS 1 – well with some symptoms

PS 2 – needing help, up for more than ½ day

PS 3 – in bed more than ½ the day

PS 4 – very unwell, needing all care

Well enough for treatment

Borderline

Not well enough for treatment

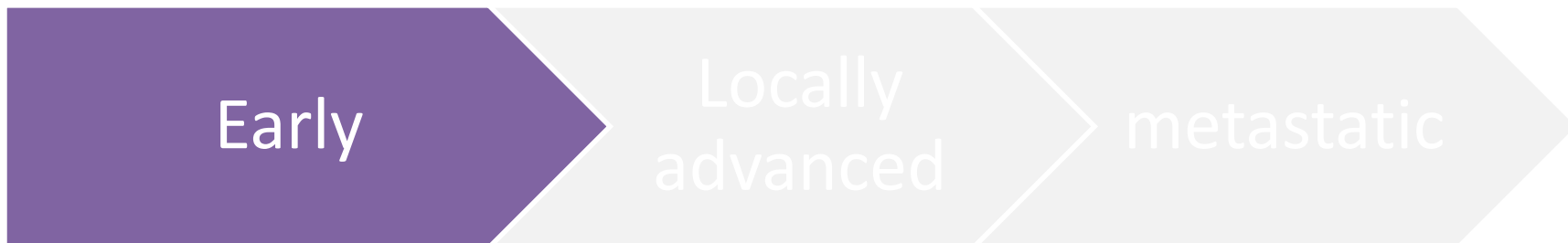
Other health problems

Other medication

Preferences

Building on our current treatments

What stage is the cancer at?



Surgery...

- Performed in specialist centres
- Aiming to remove all of the cancer
- Also removing lymph nodes next to the cancer

...followed by 6-month course of oral chemotherapy (capecitabine)

- To “mop up” any remaining cancer cells
- Reduces the chance of the cancer returning
- Improves survival

What stage is the cancer at?



- Surgery is not possible
- Treatment is the same (**chemotherapy**) as for metastatic disease (more advanced)
- It may be possible to give additional local treatment (e.g. **radiotherapy**)

Occasionally, if the disease responds well to treatment (shrinks), it may be possible to do surgery

What stage is the cancer at?

Early

Locally
advanced

metastatic

- Unfortunately, this is the majority of patients
- Current treatment is chemotherapy
- Treatment usually for 6 months
- Monitoring CT scans, blood tests, side-effects and quality of life

First-line:

- PS 0-1: cisplatin and gemcitabine
- PS2: gemcitabine alone



What stage is the cancer at?

Early

Locally
advanced

metastatic

- Unfortunately, this is the majority of patients
- Current treatment is chemotherapy
- Treatment usually for 6 months
- Monitoring CT scans, blood tests, side-effects and quality of life

Second line:

- PS 0-1: oxaliplatin and 5-fluorouracil *
- (*also known as FOLFOX or OxMdG)

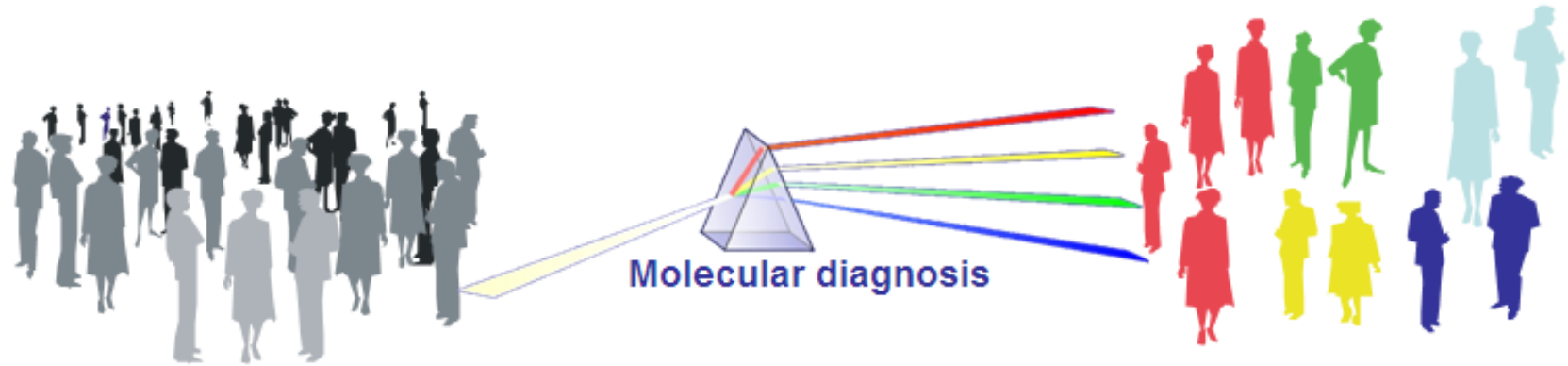


Building on our current treatments

What approaches are being tried?

- Intensifying chemotherapy (3-drug combinations)
- New drugs (like NUC-1031, Etoposide Toniribate (EDO S7.1))
- New modalities
 - Proton beam
 - HAI
 - Radioembolisation
- **Molecularly-targeted therapy**

What is precision medicine?

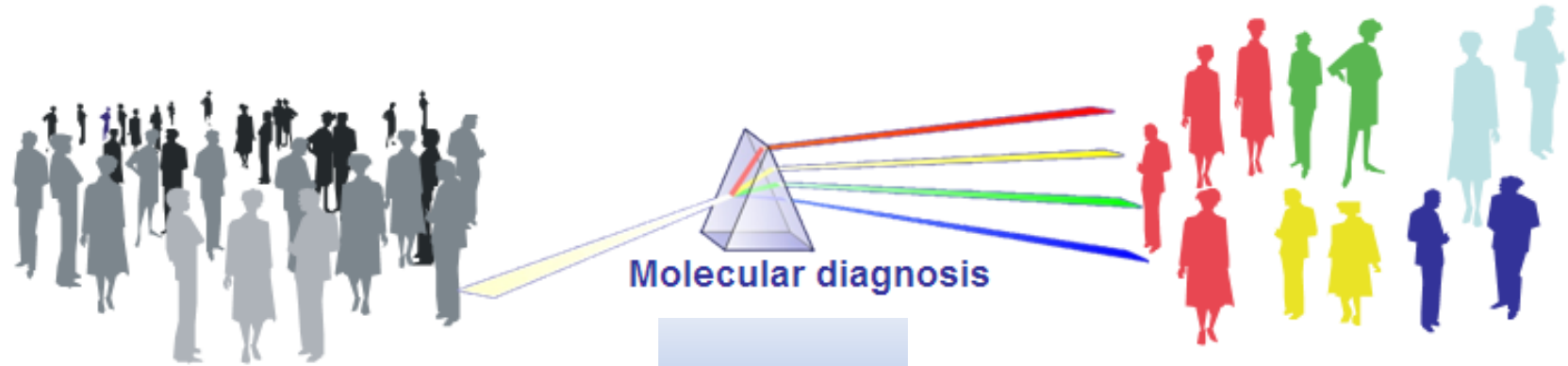


Here all patients are treated the same...

- Some respond to treatment
- Others do not

Here, patients are ***treated according to their molecular profile***, increasing the chances of benefit

What is precision medicine?



Here all patients are treated the same...

- Some respond to treatment
- Others do not

“fingerprinting” of DNA,
RNA, proteins on
TUMOUR BIOPSY

Here, patients are ***treated according to their molecular profile,*** increasing the chances of benefit

Learning a lot about the genetics of CCA

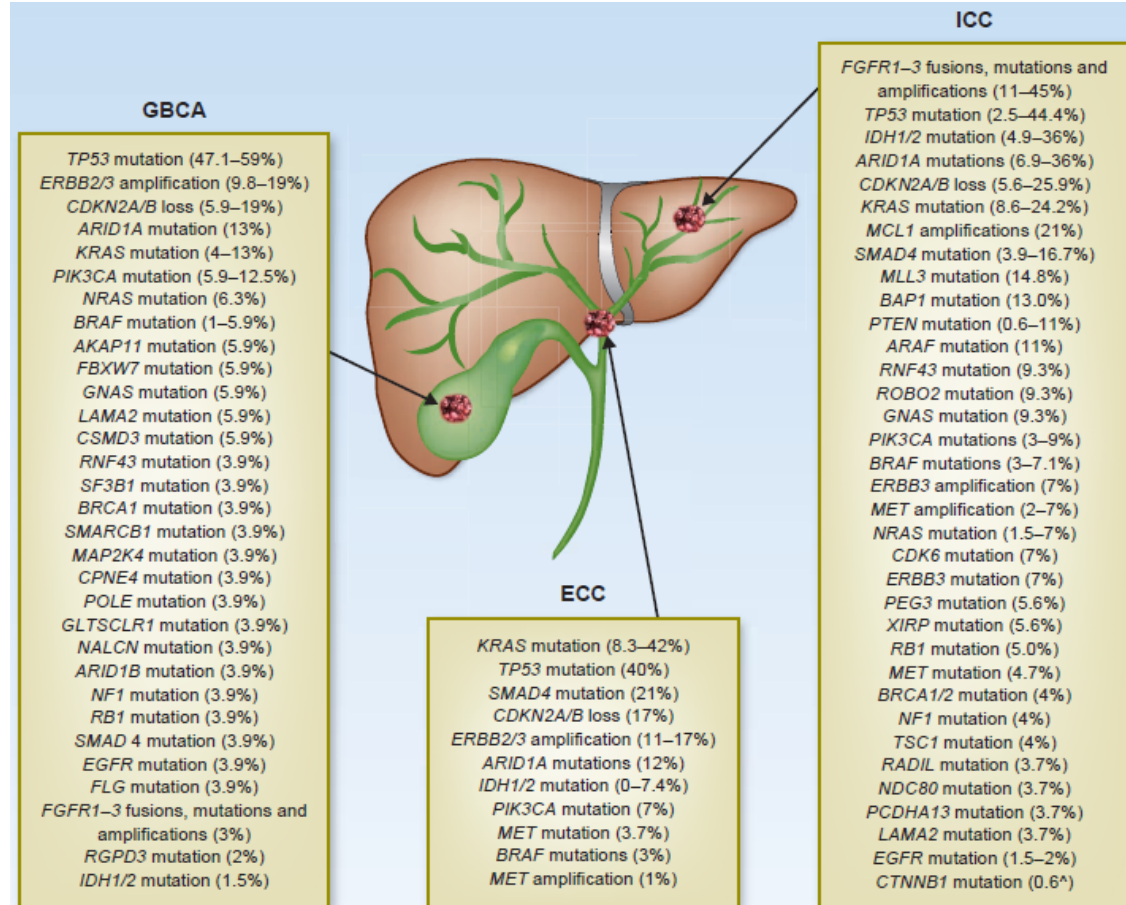
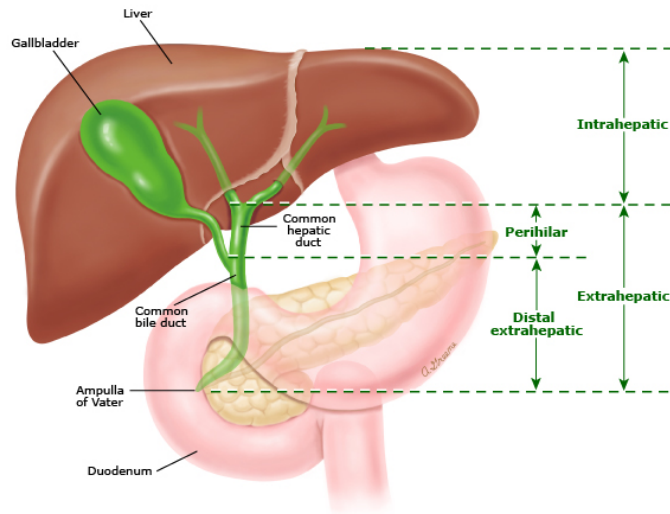


Figure from Valle et al
Cancer Discov 2017;7(9):943-962

From anatomical to molecular subgroups

Anatomical



Molecular

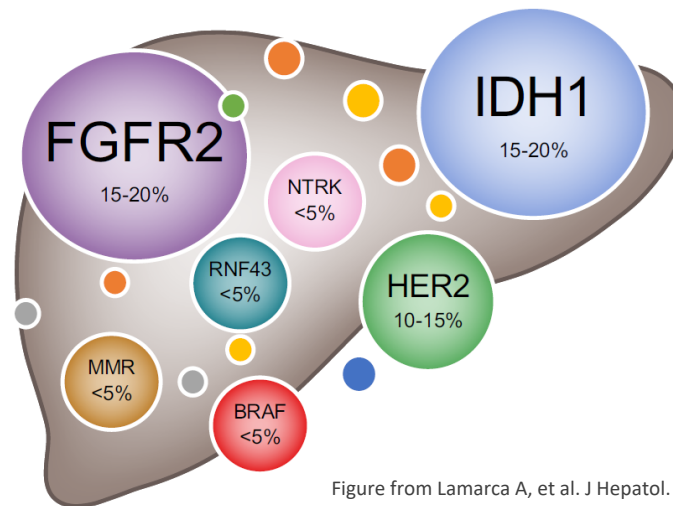


Figure from Lamarca A, et al. J Hepatol. 2020

Molecular profiling and targeted therapies



At the moment, these therapies only apply to patients with advanced disease



Looking for FGFR2 fusions

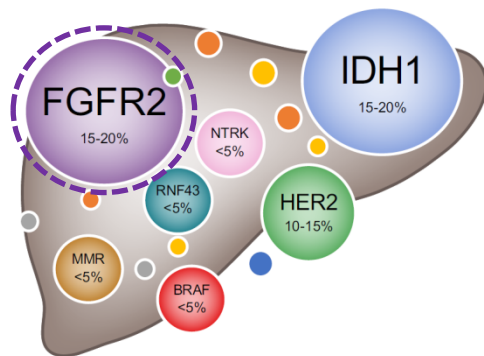
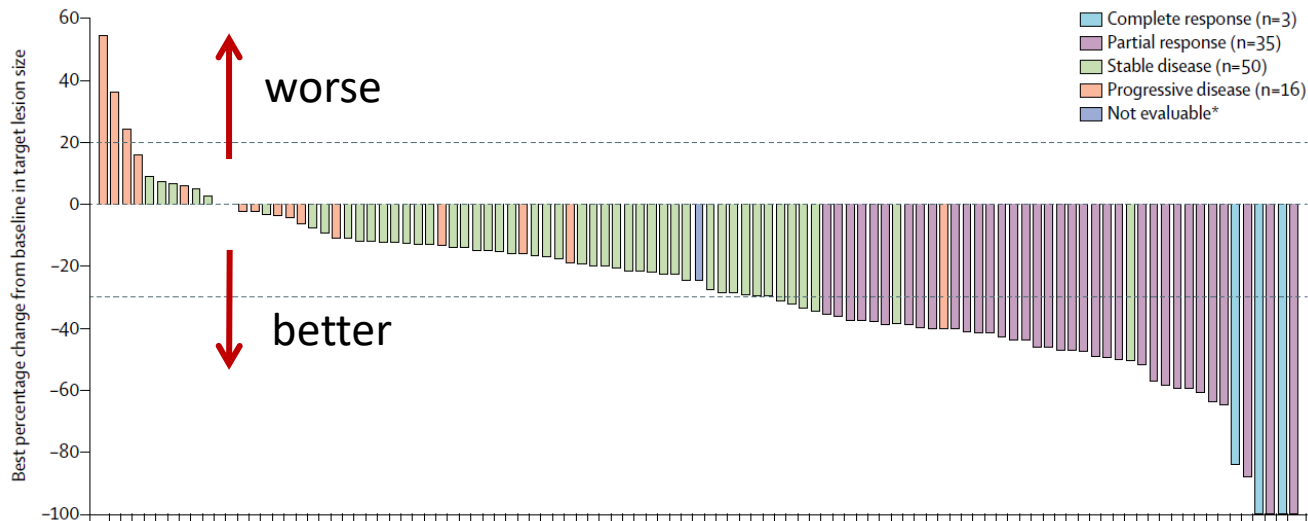


Figure from Lamarca A, et al. J Hepatol. 2020

Applies to about 10-15% of patients with iCCA

FIGHT-202 study Each bar represents 1 patient



Overall response rate 35.5%
Disease control rate 82.2%
Median Duration of Response 7.5 months

First targeted treatment approved ...in the USA



Tweet



AMMF @CharityAMMF · 24 Apr

@US_FDA has approved @Incyte's #Pemazyre (pemigatinib) for the treatment of advanced #cholangiocarcinoma, but this targeted therapy is not available in the UK or Europe. To find out why, see: ammf.org.uk/2020/04/24/fda...

#bileductcancer #cancer



1



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Relevant people



AMMF

@CharityAMMF

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AMMF is the UK's only cholangiocarcinoma (bile duct cancer) charity. Working throughout the UK and Europe, and collaborating globally.



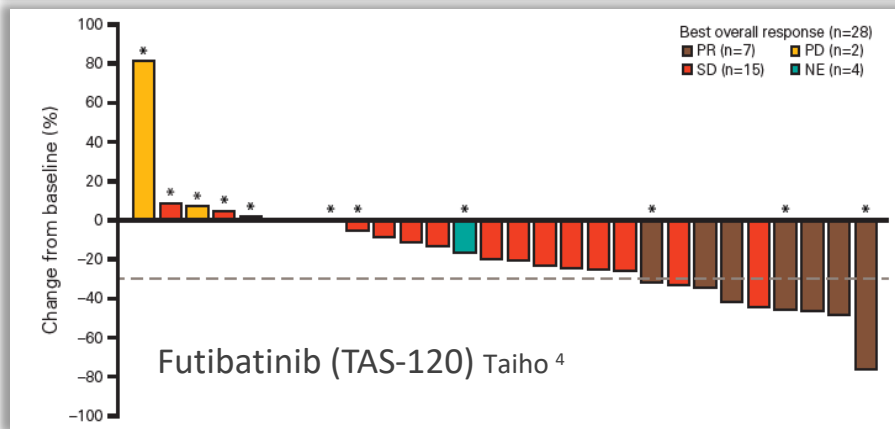
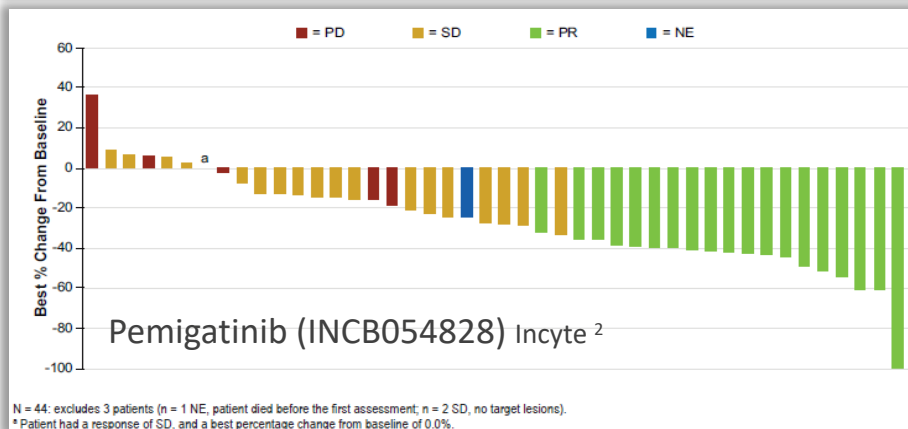
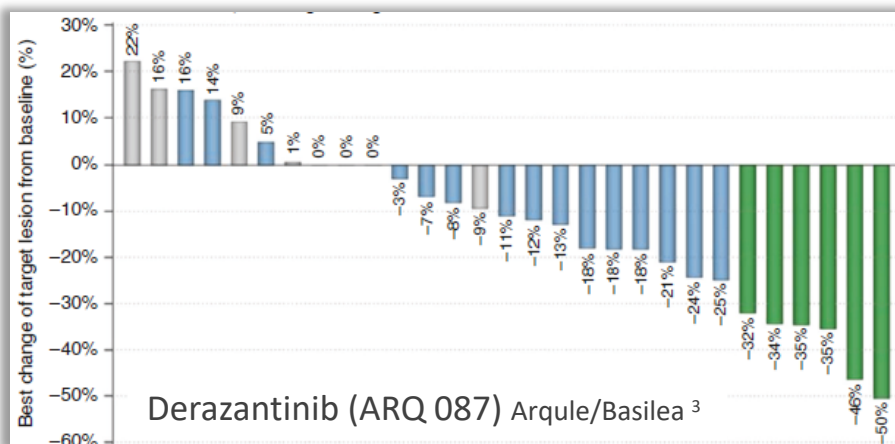
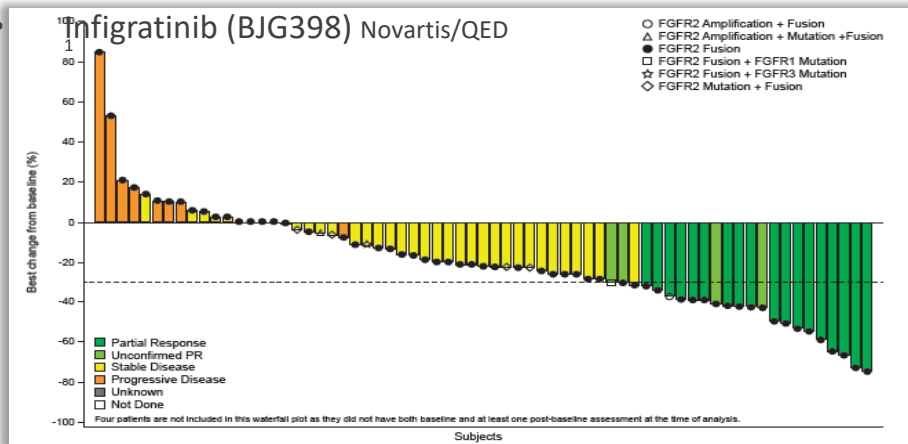
U.S. FDA

@US_FDA

Follow

Here you'll find the latest US Food and Drug Administration news and

There are many FGFR2-targeted agents



Looking for mutations in IDH1

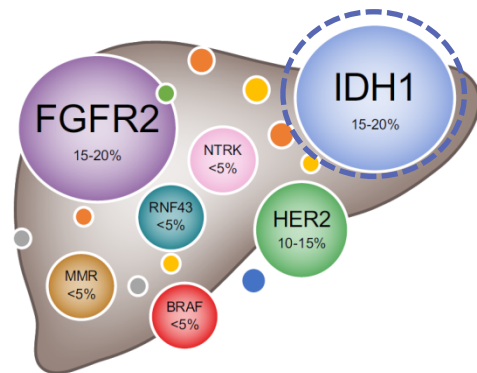
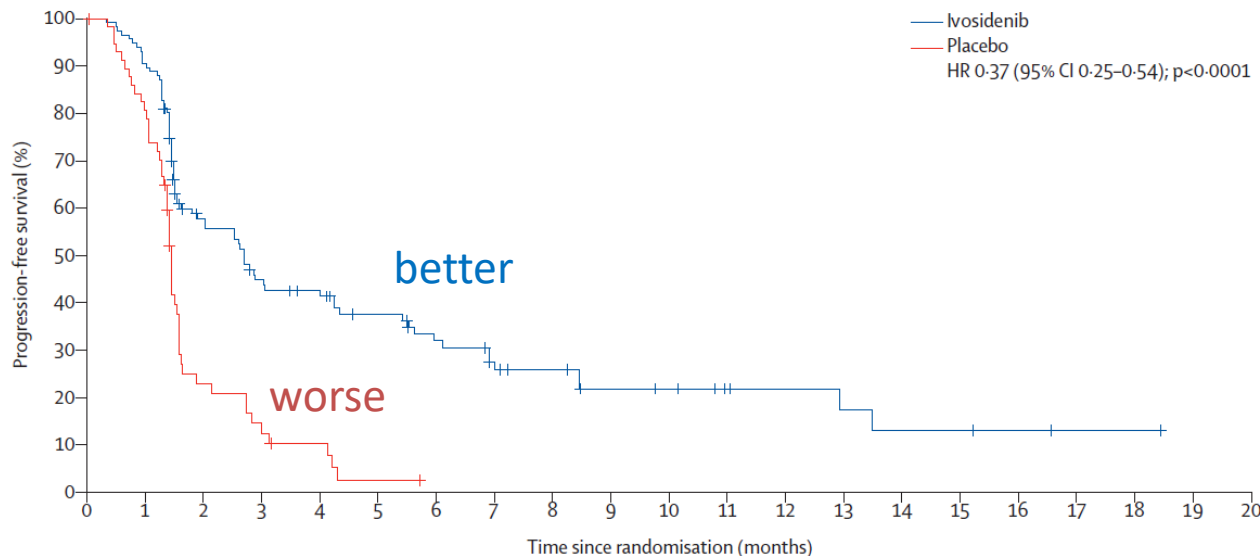


Figure from Lamarca A, et al. J Hepatol. 2020

Applies to about 10-15% of patients with iCCA

ClarIDHy study Each bar represents 1 patient



Ivosidenib delayed the cancer from getting worse by 63%

Patients were allowed to cross over

Patients receiving ivosidenib seem to live longer, but mature results are awaited

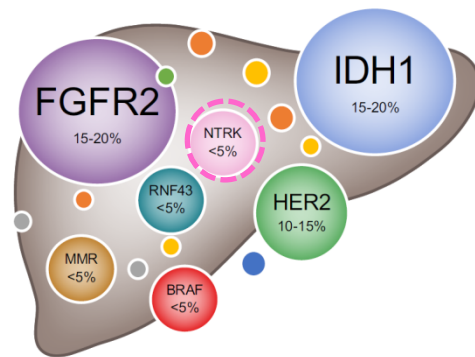


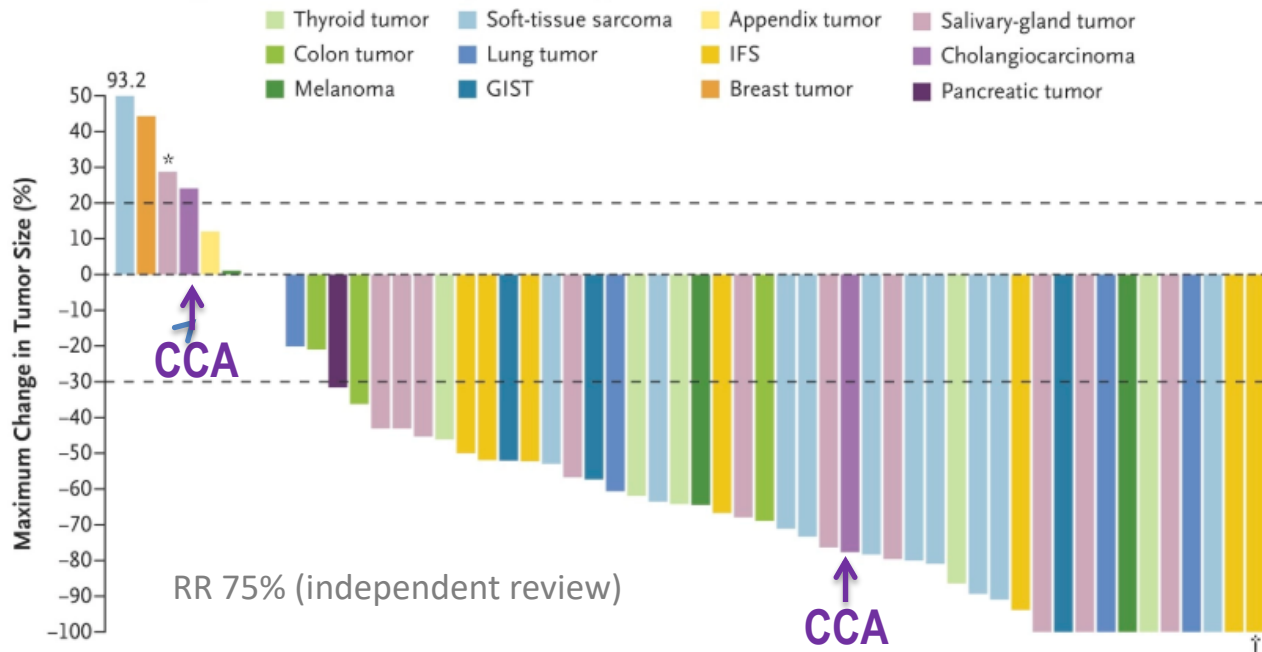
Figure from Lamarca A, et al. J Hepatol. 2020

Applies to about 3.5% of patients with CCA

Looking for NTRK fusions

neurotrophic receptor tyrosine kinase

Maximum Change in Tumor Size, According to Tumor Type



- **Nov 2018** | FDA grants accelerated approval to larotrectinib for patients with solid tumours that have a NTRK gene fusion
- STARTRK-2 study (entrectenib) recruiting [NCT02568267]

Looking for mismatch repair deficiency

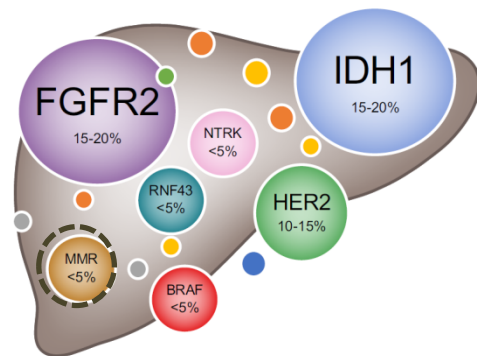
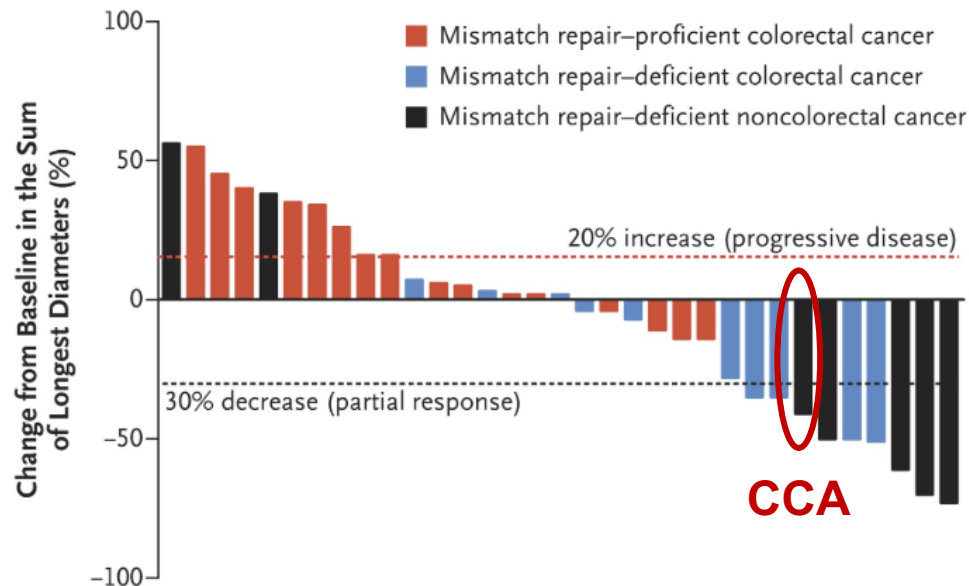


Figure from Lamarca A, et al. J Hepatol. 2020

Applies to about 2.5% of patients with CCA

B Radiographic Response



May 2017 | FDA grants accelerated approval to pembrolizumab for first tissue/site agnostic indication²

Relevant to ~2.5% of cholangiocarcinoma patients

¹ Le et al NEJM 2015; 372(26):2509-20

² <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm560040.htm>

Looking for mismatch repair deficiency

NICE National Institute for
Health and Care Excellence

Search NICE...



Sign in

NICE Pathways

NICE guidance

Standards and indicators

Evidence search

BNF

BNFC

CKS

Journals and databases

Read about [our approach to COVID-19](#)

Home > NICE Guidance > Conditions and diseases > Infections > COVID-19

COVID-19 rapid guideline: delivery of systemic anticancer treatments

NICE guideline [NG161] Published date: 20 March 2020 Last updated: 27 April 2020

Guidance

Tools and resources

Evidence

Overview

1 Communicating with patients

Guidance

[Download guidance \(PDF\)](#)

Looking for mismatch repair deficiency

NICE National Institute for
Health and Care Excellence

Search NICE...



Sign in

NICE Pathways

NICE guidance

Standards and indicators

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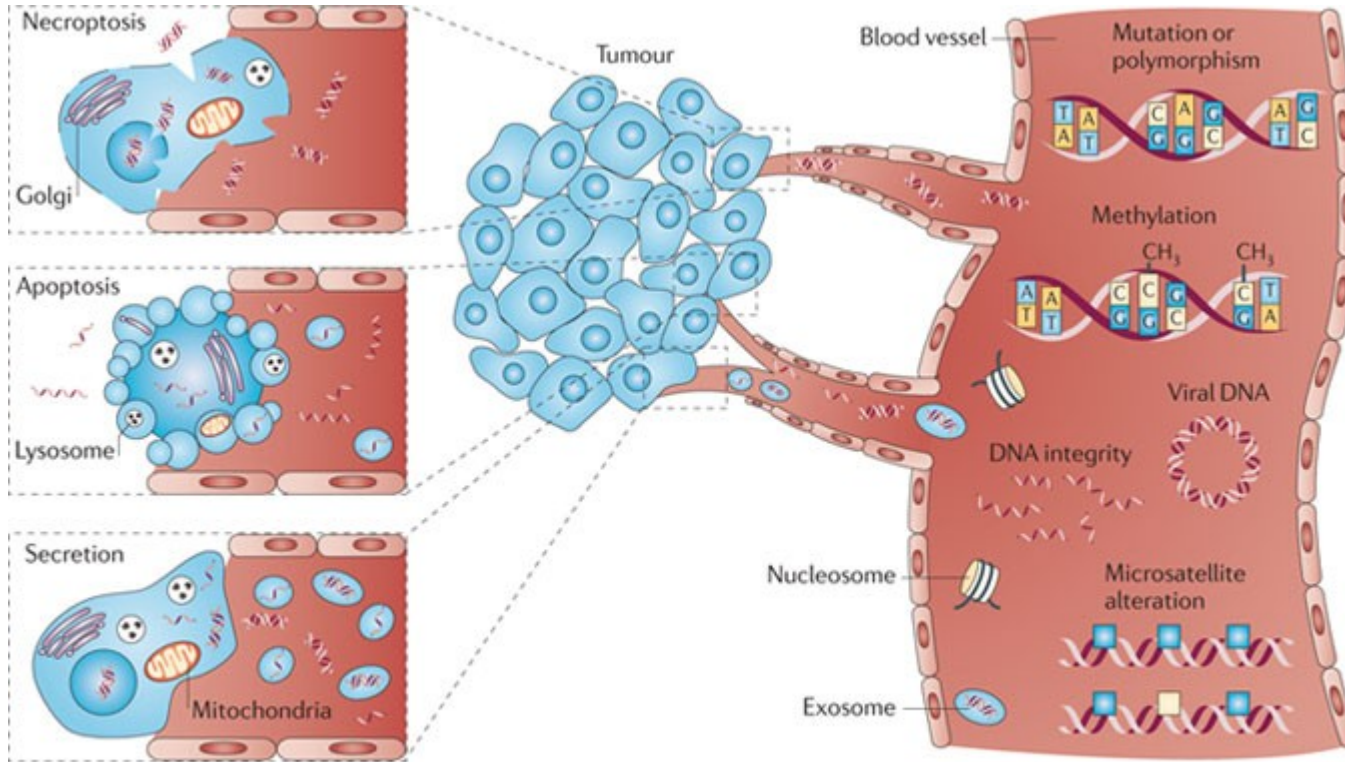
Home > NICE Guidance > Conditions and diseases > Infections > COVID-19

COVID-19 rapid guideline: delivery of systemic anticancer treatments

Upper gastrointestinal cancers (oesophageal, gastric, small bowel, biliary tract, pancreatic)

- Option to give nivolumab instead of chemotherapy for microsatellite instability-high tumours to reduce toxicity of treatment **[added 3 August 2020]**

What about a “*liquid biopsy*”

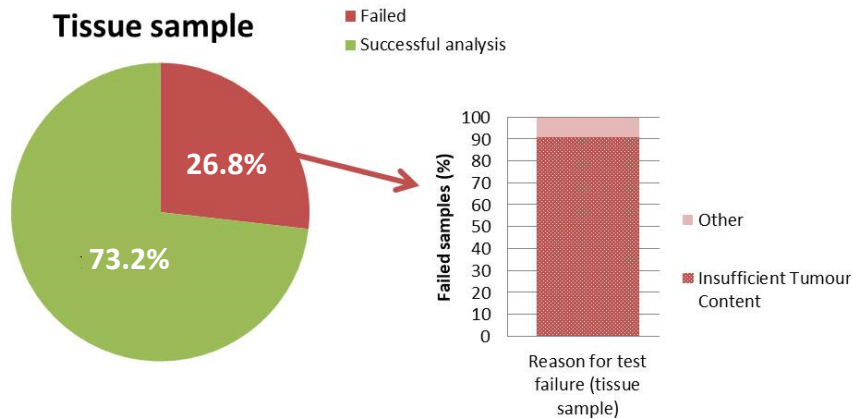


Nature Reviews | Cancer

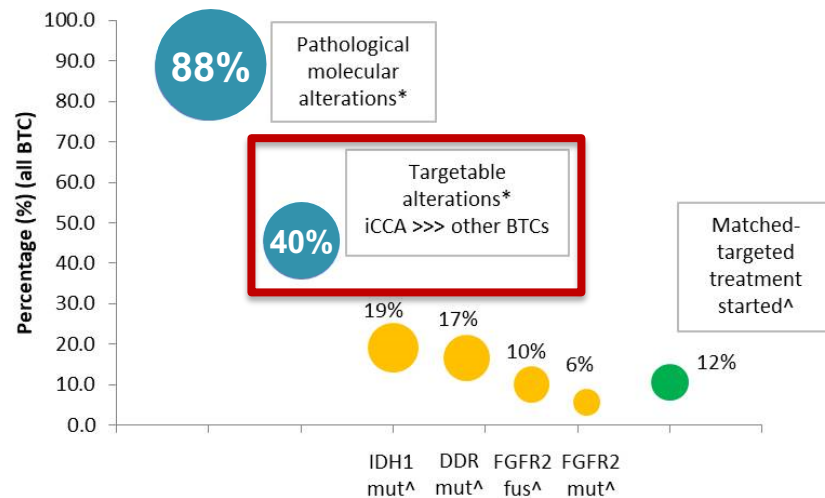
“Precision Medicine” is not possible for *ALL* Patients

- Reason #1: Quality tissue sample not always available

- Cytology-based diagnosis
- Failed tissue samples



- Reason #2: Targetable finding ~40% of patients
 - ~60%: not suitable for targeted therapies




We will still need new chemotherapy options



Text Size + -



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AMMF > Current Cholangiocarcinoma Trials

Cholangiocarcinoma

- **Introduction**

- What is Cholangiocarcinoma?
- Causes and risk factors
- Symptoms
- Diagnosis and Staging

- **Treatments**

- Treatment options
- Specialist Centres
- International Centres
- Clinical Trials
- Guidelines for Diagnosis and

Current Cholangiocarcinoma Trials

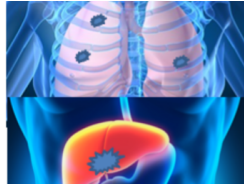
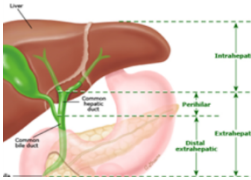
Listed here are the clinical trials for those with cholangiocarcinoma (bile duct cancer) or gall bladder cancer, currently open and recruiting in the UK.

Wherever possible links for further information have been included to follow up for more information and to check eligibility. Each trial has specific eligibility criteria, so if you are interested in taking part in one, please discuss with those running the trial (contact details are given where possible) and/or your consultant.

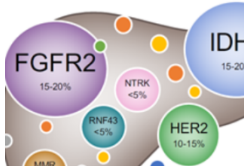
Please note it is not appropriate for AMMF to



Anatomical



Molecular



inoma Trials

cholangiocarcinoma (bile duct cancer)



Take-home messages

Every patient is an individual

- Our understanding of the biology (what makes the cancer tick) is improving
- In **early-stage** disease **surgery followed by chemotherapy** gives the best chance of cure
- **Molecular profiling** is increasingly important as it can lead to new treatment options
- We still have the other pillars of therapy: **chemotherapy** and **radiotherapy**
- **Clinical research** is accelerating and new treatments emerging
- The role of **immunotherapy** is being extensively evaluated

Acknowledgements



WORLD CHOLANGIOCARCINOMA DAY
FEBRUARY 12, 2020

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